xxxxxxxx-5343

OLANZAPINE

TOLANZ 5
TOLANZ 10
5 mg Orodispersible Tablet
10 mg Orodispersible Tablet
Antipsychotic

FORMULATION
Each orodispersible tablet contains:
Olanzapine …….. 5 mg / 10 mg
PRODUCT DESCRIPTION
Olanzapine (Tolanz 5) 5 mg orodispersible tablet and Olanzapine (Tolanz 10) 10 mg orodispersible tablet are yellow colored, round, flat, bevel edged uncoated tablets with break line on one side and plain on other side.
PHARMACODYNAMICS
Mechanism of Action:
Olanzapine is a thienobenzodiazepine atypical antipsychotic. It has affinity for serotonin, muscarinic, histamine H-1, and adrenergic (α1) receptors as well as various dopamine receptors.
PHARMACOKINETICS
Olanzapine is well absorbed from the gastrointestinal tract after oral administration but undergoes considerable first-pass metabolism. Peak plasma concentrations are achieved about 5 to 8 hours after oral administration and about 15 to 45 minutes after intramuscular administration. Olanzapine is about 93% bound to plasma proteins. It is extensively metabolized in the liver primarily by direct glucuronidation and by oxidation mediated through the cytochrome P450 isoenzymes CYP1A2 and, to a lesser extent, CYP2D6. The two major metabolites 10-N-glucuronide and 4'-N-desmethyl olanzapine appear to be inactive. About 57% of a dose is excreted in the urine, mainly as metabolites and about 30% appears in the feces. The plasma elimination half-life has been variously reported to be about 30 to 38 hours; half-lives tend to be longer in female than in male patients. Olanzapine is distributed into the breast milk.
INDICATION
Used in the management of schizophrenia and for the treatment of moderate to severe mania associated with bipolar disorder.
DOSAGE AND ADMINISTRATION
Schizophrenia: The recommended starting dose is 10mg daily.
Acute Manic Episodes: A recommended initial dose is 10 to 15mg daily by mouth as monotherapy or 10mg if given as part of combination therapy; dosage adjustments of 5mg may subsequently be made at intervals of not less than 24 hours if necessary within the range 5 to 20mg daily. If a response is achieved, therapy may continue at the same dosage to prevent recurrence.
Prevention of Recurrence: In patients whose manic episodes have responded previously to olanzapine the recommended starting dose is 10 mg daily.
Patients with Hepatic and/or Renal Impairment: A starting dose of 5mg daily by mouth may be necessary for patients with renal impairment; for patients with moderate hepatic insufficiency the starting dose should be 5mg daily, and only increased with caution.
Others: The metabolism of Olanzapine might be slower in female, elderly, or non-smoking patients; if more than one of these factors is present, a lower initial dose (e.g. 5 mg daily if given by mouth) and a more gradual dose escalation should be considered.
Mode of Administration
Olanzapine orodispersible tablet should be placed in the mouth, where it will rapidly disperse in saliva, so it can be easily swallowed. Removal of the intact orodispersible tablet from the mouth is difficult. Since the orodispersible tablet is fragile, it should be taken immediately on opening the blister. Alternatively, it may be dispersed in a full glass of water or other suitable beverage (orange juice, apple juice, milk or coffee) immediately before administration.
CONTRAINDICATIONS
Hypersensitivity to olanzapine or any of the excipients. Patients with known risk for narrow-angle glaucoma.
WARNINGS
Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as neuroleptic malignant syndrome has been reported in association with administration of antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure.
Clinical manifestations of NMS or the presence of high fever without clinical manifestations of NMS require discontinuation of all antipsychotic drugs, including olanzapine.
SAFETY EXPERIENCE IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS After analysis of placebo-controlled studies revealed an increased risk in stroke and a twofold increase in all-cause mortality. It was considered that the risk may not be confined to use dementia and should be considered relevant to any patient with a history of stroke or transient ischemic attack or other risk factors for cerebrovascular disease, including hypertension, diabetes, current smoking or atrial fibrillation.
PRECAUTIONS
Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at baseline and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when the atypical antipsychotic was discontinued: however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.
Acute symptoms such as sweating, insomnia, tremor, anxiety, nausea, or vomiting have been reported very rarely when olanzapine is stopped abruptly. Gradual dose reduction should be considered when discontinuing olanzapine. Concomitant illnesses; while olanzapine demonstrated anticholinergic activity in vitro, experience during the clinical trials revealed a low incidence of related events. However, as clinical experience with olanzapine in patients with concomitant illness is limited, caution is advised when prescribing for patients with prostatic hypertrophy, or paralytic ileus and related conditions.
The use of olanzapine in the treatment of dopamine agonist associated psychosis in patients with Parkinson's disease is not recommended. In clinical trials, worsening of Parkinsonian symptomatology and hallucinations were reported very commonly and more frequently than with placebo, and olanzapine was not more effective than placebo in the treatment of psychotic symptoms.
Transient, asymptomatic elevations of hepatic transaminases, ALT, AST have been seen occasionally, especially in early treatment. Rare postmarketing reports of hepatitis have been received. Very rare cases of cholestatic or mixed liver injury have also been reported in the postmarketing period. Caution should be exercised in patients with elevated ALT and/or AST, in patients with signs and symptoms of hepatic impairment, in patients with pre-existing conditions associated with limited hepatic functional reserve, and in patients who are being treated with potentially hepatotoxic drugs, in the event of elevated ALT and/or AST during treatment, follow-up should be organized and dose reduction should be considered. In cases where hepatitis has been diagnosed, olanzapine treatment should be discontinued.
As with other neuroleptic drugs, caution should be exercised in patients with low leukocyte and/or neutrophil counts for any reason, in patients with a history of drug-induced bone marrow depression/toxicity, in patients receiving medicines known to cause neutropenia in patients with bone marrow depression caused by concomitant illness, radiation therapy or chemotherapy and in patients with hypereosinophilic conditions or with myeloproliferative disease. Thirty two patients with clozapine-related neutropenia or agranulocytosis histories received olanzapine without decreases in baseline neutrophil counts. Neutropenia has been reported commonly when olanzapine and valproate are used concomitantly. There are limited data on co-medication with lithium and valproate. There are no clinical data available on olanzapine and carbamazepine co-therapy, however a pharmacokinetic study has been conducted.
Olanzapine should be used cautiously in patients who have a history of seizures or are subject to factors which may lower the seizure threshold. Seizures have been reported to occur rarely in patients when treated with olanzapine. In most of these cases, a history of seizures or risk factors for seizures were reported.
Given the primary CNS effects of olanzapine, caution should be used when it is taken in combination with other centrally acting drugs and alcohol. As it exhibits in vitro dopamine antagonism, olanzapine may antagonize the effects of direct and indirect dopamine agonists. As with other antipsychotics, it is recommended that blood pressure is measured periodically in patients over 65 years.
Olanzapine may affect the performance of skilled tasks such as driving.
PREGNANCY & LACTATION
Pregnancy: There are no adequate and well-controlled studies in pregnant women. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with olanzapine. Nevertheless, because human experience is limited, this drug should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.
Spontaneous reports have been very rarely received on tremor, hypertonia, lethargy and sleepiness, in infants born to mothers who had used olanzapine during the 3rd trimester.
Lactation: Patients should be advised not to breast feed an infant if they are taking olanzapine.
DRUG INTERACTIONS
The central effects of other CNS depressants including alcohol may be enhanced by Olanzapine. Olanzapine may antagonize the actions of dopaminergics. Neutropenia may be more common when olanzapine is given with valproate. There is a theoretical risk of QT prolongation when olanzapine is given with other drugs that are known to cause this effect.
The metabolism of Olanzapine is mediated to some extent by the cytochrome P450 isoenzyme CYP1A2. Use with drugs that inhibit, induce, or act as a substrate to this isoenzyme may affect plasma concentrations of olanzapine and a dose adjustment of olanzapine may be required. The CYP1A2 inhibitor of fluvoxamine significantly inhibits the metabolism of Olanzapine. The clearance of Olanzapine is increased by tobacco smoking and carbamazepine.
ADVERSE REACTIONS
The most frequent adverse effects with Olanzapine are somnolence and weight gain; hyperprolactinemia is also common, but usually asymptomatic. Increased appetite, dizziness, elevated plasma glucose, triglyceride, and liver enzyme values, eosinophilia, edema, orthostatic hypotension, and mild transient antimuscarinic effects such as constipation and dry mouth are also relatively common. Speech difficulty has also been reported. More severe abnormalities of glucose homeostasis occur uncommonly; severe hyperglycemia, or exacerbation of pre-existing diabetes, sometimes leading to ketoacidosis or coma, has been reported. Clinical monitoring for hyperglycemia has been recommended, especially in patients with or at risk of developing diabetes. Olanzapine has been associated with a low incidence of extrapyramidal symptoms including tardive dyskinesia although extrapyramidal symptoms may be more likely at high doses. Neuroleptic malignant syndrome has been reported rarely.
For suspected adverse drug reaction, report to FDA: www.fda.gov.ph or to TORRENT: www.torrentpharma.com".
Patient to seek medical attention immediately at the first sign of any adverse drug reaction shall appear.
OVERDOSAGE AND TREATMENT
Very common symptoms in overdose include tachycardia, agitation, aggressiveness, dysarthria, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. Other medically significant sequelae of overdose include delirium, convulsion, coma, possible neuroleptic malignant syndrome, respiratory depression, aspiration, hypertension or hypotension, cardiac arrhythmia and cardiopulmonary arrest. Fatal outcomes have been reported for acute overdoses as low as 450 mg but survival has also been reported following acute overdose of 1,500 mg.
Management of Overdose
There is no specific antidote for olanzapine. Induction of emesis is not recommended. Standard procedures for management of overdose may be indicated (e.g. gastric lavage, administration of activated charcoal). The concomitant administration of activated charcoal was shown to reduce the oral bioavailability of olanzapine by 50 to 60%. Symptomatic treatment and monitoring of vital organ function should be instituted according to clinical presentation, including treatment of hypotension and circulatory collapse and support respiratory function. Do not use epinephrine, dopamine, or other sympathomimetic agents with beta-agonist activity since beta stimulation may worsen hypotension. Cardiovascular monitoring is necessary to detect possible arrhythmia. Close medical supervision and monitoring should continue until the patient recovers.
CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
STORAGE AND CONDITION
Store at temperatures not exceeding 30^{o}C.
AVAILABILITY
Olanzapine (Tolanz 5) 5 mg orodispersible Tablet - Alu-Alu blister pack of 10's (Box of 30's) - DRP - 5804
Olanzapine (Tolanz 10) 10 mg orodispersible Tablet - Alu-Alu blister pack of 10's (Box of 30's) - DRP - 5805
DATE OF FIRST AUTHORIZATION
March 20, 2012
DATE OF REVISION
May 2016

torrent PHARMA

Manufactured by :
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PRODUCT NAME :	Tolanz	**COUNTRY :** Philippines	**LOCATION :** Chhatral	**Supersedes A/W No.:**			
ITEM / PACK :	Insert	**NO. OF COLORS:** 1	**REMARK :**				
DESIGN STYLE :	Front-Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**				
CODE :	xxxxxxxxx-5343	Black	**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM) :	150 x 220		Prepared By	**Pkg.Dev**			
ART WORK SIZE :	S/S		Reviewed By	**Pkg.Dev**			
DATE :	09-01-2018		Approved By	**Quality**			